Late-onset limb-girdle muscular dystrophy caused by GMPPB mutations.

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Abstract
Mutations in GMPPB gene have been reported in patients with early-onset disease ranging from severe congenital muscular dystrophies to limb-girdle muscular dystrophy (LGMD) with mental retardation. More recently mutations in GMPPB have been identified with congenital myasthenic syndromes as well as milder phenotypes. We report two unrelated cases with LGMD that underwent clinical, histopathological and genetic studies. In both cases, we found identical compound heterozygous GMPPB mutations c.79G>C p.D27H and c.859C>T p.R287W, leading to a glycosylation defect of alpha-dystroglycan. The onset of muscle weakness was 30-40 years and the progression rate mild to moderate. Case 2 became wheelchair-bound at the age of 60. No cognitive or behavioral symptoms were noted. These cases provide further evidence that GMPPB mutations can also cause late-onset recessive LGMD with milder phenotypes than previously reported, and thus should be considered in the differential diagnosis of patients with adult-onset muscular dystrophies.

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KEYWORDS: Alpha-dystroglycan; GMPPB gene; Late-onset; Limb-girdle muscular dystrophy

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